Scientific Abstract

Severe combined immunodeficiency (SCID) due to deficiency of the purine metabolic enzyme adenosine deaminase (ADA) is a fatal childhood immunodeficiency disease. Immune reconstitution by transplantation with HLA-identical bone marrow is the treatment of choice. For patients not candidates for bone marrow transplantation, we propose to attempt immune reconstitution by using infusions of autologous T lymphocytes expanded in tissue culture and genetically corrected by insertion of a normal ADA gene using retroviral-mediated gene transfer. The vector is LASN, in which the human ADA gene is promoted by the LTR while the NeoR gene is driven by the SV40 early gene promoter. The packaging line is PA317.

The protocol is designed to have two parts. In Part 1, autologous gene-corrected T lymphocytes would be infused repeatedly in low numbers in order to build an immune repertoir of T cells and also to obtain information as to how long gene-corrected T cells survive in vivo. In Part 2A, the gene-corrected T cells would be selected in G418 and/or 2'deoxyadenosine and reinfused into the patient at monthly intervals for approximately six months. The goals would be essentially the same as in Part 1. In Part 2B, the number of gene-corrected T cells would be escalated in half-log increments to the predicted therapeutic level (probably around 1 x 10^9/kg). 1-3 x 10^9/kg gene-corrected cells would be infused several times and the patient would be monitored in order to determine if significant clinical improvement has occurred.